I.1 Measurement of renal function

Guideline I.1.1

A. Renal function should not be estimated from measurements of blood urea or creatinine alone. Cockcroft and Gault equation or reciprocal creatinine plots should not be used when the glomerular filtration rate (GFR) is <30 ml/min or to determine the need for dialysis. (Evidence level: A)

Guideline I.1.2

A. To reduce confusion when communicating with general physicians and to encourage timely referral of patients with renal failure:

Renal function should be reported as GFR equivalent (ml/min/1.73 m²). (Evidence level: C)

Dialysis terms such as Kt/V and weekly creatinine clearance should be avoided. (Evidence level: C)

Guideline I.1.3

A. GFR should only be estimated using a method, which has been validated in patients with advanced renal failure. The preferred method for calculating GFR in advanced renal failure is the mean of urea and creatinine clearance. The latter is best calculated from a 24-h urine collection and normalized to 1.73 m². (Evidence level: C)

B. Other examples of validated GFR estimations are:

- MDRD equation
- Indicator decay methods (e.g. iohexol, iothalamate, EDTA, inulin)
- Creatinine clearance after oral cimeticidine

Guideline I.1.4

A. To assist in the standard reporting of renal function in advanced renal failure, the preferred methods of estimating GFR in advanced renal failure are EITHER:

- MDRD equation (Evidence level: B) (Appendix I)

OR

The mean of urea and creatinine clearance, calculated from 24-h urine collections and normalized to 1.73 m²; preferably using the Gehan and George method for calculating surface area. (Evidence level: B) (Appendix I)

Guideline I.1.5

A. To assist in the detection and timely referral of patients with renal failure, laboratories should be encouraged to report the GFR using the MDRD equation when serum creatinine above the normal
range is measured and there is insufficient data to calculate GFR more directly.  
(Evidence level: C)

B. If creatinine clearance is requested from a 24-h urine collection, the laboratories should also report GFR calculated from the mean of urea and creatinine clearance. The report should indicate that this GFR is not normalized for surface area and should show indicative normal ranges for different sized patients.  
(Evidence level: C)

Commentary on Guidelines I.1.1–I.1.5

Serum creatinine or reciprocal serum creatinine in patients with advanced renal failure are an unreliable measure of renal function and progression of renal failure [5–16]. This is due to differences in muscle mass associated with age, gender, race, nutrition, activity, and disease. Creatinine generation rate declines as renal disease progresses and the serum creatinine may not predictably reflect renal function [17].

The serum concentrations of both urea and creatinine have been shown to relate to mortality—the lower the concentration, the higher the mortality [18–21]. This is probably because, in patients with renal failure, a lower serum creatinine is more a marker of inactivity and malnutrition than it is of adequate renal function. On the other hand, low renal clearance at initiation of dialysis is significantly related to high renal function. On the other hand, low renal clearance of inactivity and malnutrition than it is of adequate renal function. On the other hand, low renal clearance at initiation of dialysis is significantly related to high renal function. On the other hand, low renal clearance at initiation of dialysis is significantly related to high renal function.

GFR normalized to surface area and expressed in units of ml/min/1.73m² is recognized as the standard measurement of renal function [24]. Numerous different methods for quantifying renal function have been validated against ‘gold-standard’ GFR measurements. The most accurate and direct measurements of GFR require timed blood sampling after administration of a tracer. This is often impractical for routine use in the nephrology clinic and is unrealistic as a standard for general practice. More practically, an estimate of GFR can be calculated from timed urine collections and a blood sample. As creatinine is secreted into the urine by the renal tubules, creatinine clearance overestimates GFR in advanced renal failure by as much as 70% [5,25]. By chance, the renal tubules absorb urea so that the mean of urea and creatinine clearance is close to GFR (actually underestimating GFR by ~10%) [5,26,27]. In CAPD, the standard method of quantifying residual renal function is by 24 h urine collection, calculating GFR as the mean of urea and creatinine clearance and normalizing to 1.73 m² surface area. This method has been the most well studied in advanced renal failure both before starting dialysis and after starting CAPD [22].

Alternatively, tubular creatinine secretion may be blocked by oral cimetidine, so that GFR can be estimated directly from creatinine clearance [5,25].

The accuracy of urine-based GFR estimation is dependent on the patient collecting the urine properly over a defined time. Common sources of error include; failing to empty the bladder at the start of the collection, failing to collect all urine passed during the collection interval, and errors in timing the interval. In theory, these errors can be minimized if the patient is carefully and consistently instructed and if duplicate measurements are made.

Urine-based GFR estimation requires normalization to surface area. The Gehan and George [28] method for calculating surface area is preferred, as it has been validated in 400 subjects [29]. It is recognized that the alternative Dubois and Dubois equations [30] for predicting surface area are widely used (including in the MDRD study) although were based on only nine subjects.

In order to avoid these practical difficulties, many nephrologists estimate the GFR using the Cockcroft and Gault method, which uses serum creatinine. Age, gender, and body weight are used to correct for the differences in muscle mass, and hence creatinine generation rate. This method gives reasonable agreement with GFR in mild degrees of renal failure (GFR ~ 50 ml/min) but overestimates GFR by up to 100% when GFR is 10 ml/min [5] or less. This is presumably because the relative malnutrition and inactivity in advanced renal failure results in additional decline in creatinine generation rate. As there is a better alternative (see below), the Cockcroft and Gault method should no longer be used.

The MDRD study [5] demonstrated that GFR could be estimated reliably in advanced renal failure using blood and demographic data. The MDRD method requires age, gender, race (black or white), and serum urea, creatinine and albumin. A simplified version of the MDRD method dispenses with the urea and albumin with a slight reduction in accuracy. Clinical chemistry laboratories generally have access to all the data apart from race. If race is unavailable and white race may be assumed, GFR will be underestimated by 18% if the patient is black (Afro-Caribbean). In the MDRD study, the equation predicted GFR at least as precisely as the mean of urea and creatinine clearance in 24-h urine collections.

The GFR calculated using the MDRD method is already corrected for surface area and requires no measurement of weight or additional normalization. It should be noted that the MDRD equation has only been validated in American black and white racial groups. A patient categorized as black had a higher creatinine generation rate than one categorized as white and the equations reflect this difference. It is not yet clear how well the MDRD equations predict GFR in Asians or other racial groups. Until the method has been validated in other non-white racial groups, the MDRD equation should be used assuming white race and the resulting GFR prediction interpreted with caution.

The MDRD study based its conclusions on measurement of serum creatinine by the enzymatic
method, which is specific for creatinine. The commonly used Jaffe method for measuring creatinine is known to be subject to interference from certain drugs, glucose, and ketoacids. The Jaffe method may overestimate creatinine by ~8%, depending on the clinical and laboratory factors. Ideally, creatinine should be measured by a specific method such as the enzymatic method. If creatinine is measured by the Jaffe method the results should be corrected in consultation with the laboratory and interpreted with caution.